in the elderly, and the need to take the drug for a long period have limited its prescription. Similarly, medroxyprogesterone given in selected cases of predominantly central or mixed sleep apnea syndrome has proved efficacious, probably because of its effect on central respiratory drive and its diuretic effect. It also helps obese patients who have a combination of obesity-hypoventilation syndrome during sleep and heavy snoring with obstructive hypopnea. The prescribed daily dosage varies between 60 and 150 mg.

In conclusion, medical treatment may be effective for mild to moderately severe sleep apnea syndromes, particularly if imaging does not indicate a significant narrowing of the oropharyngeal airway during the awake state and if a patient is not excessively obese. A combination of treatments can be considered after a complete investigation. The most common are weight loss with or without low-flow oxygen and medroxygesterone, weight loss with or without low-flow oxygen and protriptyline (less frequently prescribed because of the eventual increase in appetite with protriptyline) and L-tryptophan and low-flow oxygen.

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Adverse Drug Interactions With Theophylline

SEVERAL DRUGS can increase the activity of the hepatic cytochrome P-450 system, resulting in a more rapid elimination of theophylline. The serum level of theophylline may thereby be decreased, and inadequate control of bronchospasm can be expected. The dosage requirements of theophylline may be almost doubled with heavy smoking of marijuana or cigarettes and a return to normal may gradually occur over many weeks after smoking cessation. Other drugs that clearly increase theophylline elimination are phenytoin, which may reduce the serum theophylline level by 75% if given for ten days, and phenobarbital, which has less effect. A diet high in charbroiled protein or where there is a significant reduction in coffee intake can cause an increase in the rate of theophylline excretion. In contrast, theophylline use may cause a reduction in the serum concentration of phenytoin or lithium when given with either of these drugs, and their dosages may need to be increased.

Drugs that impair hepatic excretion of theophylline include cimetidine, troleandomycin, erythromycin, allopurinol (when given in a dose of 600 mg a day for at least two weeks) and possibly propranolol hydrochloride. Only cimetidine and troleandomycin are of major concern as theophylline serum concentrations can be doubled by using these drugs, thereby resulting in the possibility of severe theophylline toxicity. Erythromycin can cause less of an effect, but clinical vigilance should be heightened when giving this antibiotic concurrently.

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Current Treatment of Pulmonary Tuberculosis

IN THE TREATMENT of pulmonary tuberculosis, isoniazid in combination with ethambutol is successful in 95% of patients who complete 18 to 24 months of chemotherapy. Although these statistics are excellent, actual results achieved have fallen short of this ideal. The major reason for treatment failure is related to neither the organisms nor the drugs but rather to lack of patient compliance. It has been shown that about 25% of patients do not complete 18 months of therapy. This frequency of premature termination of treatment, among other reasons, stimulated research into shorter courses of chemotherapy. Before the advent of rifampin, however, all attempts to shorten the duration of chemotherapy for tuberculosis resulted in unacceptably high relapse rates.

The bacteriologic basis of chemotherapy for tuberculosis is best understood by considering two populations of organisms: a rapidly dividing group of extracellular organisms and a more slowly growing pool in solid caseous material and within macrophages. Chemotherapy must be prolonged to effectively sterilize this latter pool of "persisting" organisms. Rifampin seems to be uniquely effective against this population of slow or intermittently active organisms, as shown in simulated conditions of intermittent growth in vitro. Field trials in many parts of the world have demonstrated the efficacy of 9- to 12-month regimens containing isoniazid and rifampin, with reported relapse rates of less than 5%.

Isoniazid (10 mg per kg of body weight to a maximum dose of 300 mg a day) taken orally, plus rifampin (10 mg per kg to a maximum dose of 600 mg a day) taken by mouth daily for 9 to 12 months, and for a minimum of 6 months after proved bacteriologic sputum conversion, are now recommended for initial treatment of persons with uncomplicated pulmonary tuberculosis due to drug-susceptible organisms. For persons in whom there is suspicion that the disease is caused by isoniazid-resistant organisms (such as those who have immigrated from an area of high prevalence of primary isoniazid resistance), it is necessary to begin therapy with three drugs, adding ethambutol (15 mg per kg), until results of drug susceptibility tests are available. Except for patients with renal insufficiency, ethambutol adds little to the toxicity of the regimen and offers a safeguard against the possible development of resistance to both isoniazid and rifampin. If susceptibility to all drugs is shown, ethambutol may then be discontinued. At present, short-course chemotherapy cannot be recommended for tuberculosis caused by drug-resistant organisms. If supervision can be insured, then the isoniazid-rifampin regimen may be modified

without loss of efficacy by administering the drugs daily for one to two months, then twice a week for seven to eight months. When given twice a week, the isoniazid dosage should be 15 mg per kg and rifampin, 10 mg per kg, to maximum doses of 600 mg.

With the use of isoniazid and rifampin, 90% to 95% of patients can be expected to have negative sputum cultures after three months of therapy. Bacteriologic evaluation should be done at this three-month juncture to determine if conversion has occurred. Persistently positive sputum cultures may suggest poor compliance or drug resistance. In some patients who have extensive disease, sputum conversion may take longer. Therapy may be stopped six months after sputum conversion, though it may be wise to continue for longer periods if there is continuing radiographic resolution.

Although there is no definite evidence for an increased risk of hepatotoxic effects with this regimen, some authorities recommend that it not be used in persons with acute hepatitis or severe underlying liver disease. Alcohol ingestion should be discouraged but is not a contraindication to using isoniazid and rifampin.

To date, there is little information on the use of rifampin in children, but preliminary data suggest that the nine-month isoniazid and rifampin regimen is equally efficacious and nontoxic if the previously described doses are used. Toxic effects on the liver appear to be more common with rifampin doses of 15 mg per kg of body weight or more.

Finally, although relapse rates have been remarkably low (1% to 4%), short-course therapy is still new and long-term follow-up data are not available. Until more information becomes available, patients should continue to be evaluated for 12 months after discontinuance of therapy. A review of symptoms, a chest roentgenogram and bacteriologic examination of sputum at 6 and 12 months should suffice to document a successful outcome.

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Invasive Diagnostic Approaches to Pulmonary Infiltrates

PATIENTS CAN PRESENT with focal or diffuse pulmonary infiltrates as a manifestation of either specific pulmonary or general systemic disease. Infiltrates can appear patchy, nodular or dense. The most common causes of pulmonary infiltrates are acute infection, tumor and the many disorders that cause chronic diffuse infiltrative lung disease. In essence, findings on a chest roentgenogram are almost always nonspecific and the initial diagnosis depends on the clinical setting, results of laboratory tests (cultures and cytologic and serologic tests) or the response to empiric therapy. The great majority of patients with pulmonary infiltrates have straightforward infectious pneumonia or their disorder is diagnosed by other (noninvasive) tests.

Patients in whom an invasive diagnostic approach may be necessary include those with possible infectious disease who are unresponsive to empiric therapy after a reasonable period of time (days to weeks); immunocompromised patients (including those with the acquired immune deficiency syndrome [AIDS]) with suspected pulmonary infection of unknown cause; those in whom there is a high probability of neoplasm, and patients who have chronic diffuse infiltrative lung disease. Invasive diagnostic pulmonary procedures are appropriate only when there is the expectation that the findings may significantly alter treatment plans.

Three primary ways to obtain a pulmonary tissue specimen are percutaneous needle aspiration biopsy, fiberoptic bronchoscopy and open-lung biopsy. Trephine and needle core biopsy are less useful because of increased complication rates.

The choice of technique depends on four factors, the first being the type of specimen desired and the quality and location of the infiltrate. A percutaneous needle aspiration biopsy produces a cytologic specimen with insufficient tissue to show histopathologic architecture. (Newer aspirating needles may produce useable tissue.) It is an excellent technique for diagnosing infection or neoplasm in peripheral nodules. For diffuse infiltrates wherein infection is suspected the procedure can be done at the bedside without fluoroscopy. Obviously, chronic diffuse infiltrative lung disease cannot be diagnosed by this technique. Fiberoptic bronchoscopy using a Bartlett catheter can provide accurate bacterial diagnosis (aerobic and anaerobic) of lower respiratory tract infections. Bronchoalveolar lavage is remarkably productive in diagnosing infection and is currently the technique of choice in diagnosing *Pneumocystis* pneumonia in patients with AIDS (80% to 90% yield). Transbronchial biopsy can diagnose sarcoidosis in 60% to 85% of patients but is less effective for diagnosing chronic diffuse infiltrative lung disease (35% to 40%). A transbronchial biopsy in an immunocompromised host with pulmonary infiltrates of unknown cause provides a specific diagnosis in only 25% to 30% of patients. Open-lung biopsy is the gold standard: A large piece of tissue can be obtained for culture and histopathologic examination and the surgeon has an opportunity to grossly examine part of the lung. Not all areas are sampled, however, and the results are often nonspecific (5% to 10%), especially in immunocompromised patients with diffuse pulmonary infiltrates (45%).

Second, the choice of technique is greatly affected by the tempo of disease or of patient deterioration. If the process is explosive or a patient is regressing into respiratory failure, open-lung biopsy is often the *initial* procedure of choice. Such situations encourage earlier attempts at diagnosis.

Third, risks must be considered. Percutaneous needle aspiration biopsy has an associated death rate of about 0.1%. In 25% of patients a pneumothorax develops